UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF MISSOURI
EASTERN DIVISION

UNITED STATES OF AMERICA,

Plaintiff,

v.

ERIC ANTHONY NEPUTE,
individually, and as
Owner of Quickwork LLC; and

QUICKWORK LLC,
a limited liability company,
also d/b/a WELLNESS WARRIOR,

Defendants.

Case No.: _____

DECLARATION OF RICHARD BRUCE VAN BREEMEN, Ph.D.

Pursuant to 28 U.S.C. § 1746, I declare as follows:

1. My name is Richard Bruce van Breemen, Ph.D. I am a United States citizen over the age of 18. I make this Declaration based upon my personal knowledge and, if called, I would testify to the same.

2. This declaration is made in support of a motion by the Department of Justice ("DOJ") for injunctive relief against Defendants Quickwork LLC, also doing business as Wellness Warrior, and Eric Anthony Nepute. I have personal knowledge of the matters contained herein and, if called as a witness, I could and would competently testify as to them.

QUALIFICATIONS, COMPENSATION, AND TESTIMONIAL EXPERIENCE

3. As detailed in my *curriculum vitae*, a true, correct, and complete copy of which is attached as **Attachment A**, I hold a Ph.D. in Pharmacology and currently serve as Professor of Pharmaceutical Sciences at the College of Pharmacy and as a Principal Investigator of the Linus Pauling Institute at Oregon State University.

4. My responsibilities in these positions include teaching pharmaceutical sciences, supervising graduate and post-doctoral pharmaceutical science students, and directing and leading investigations and studies into the role that vitamins, essential minerals, and chemicals from plants play in human aging, immune function, and chronic disease processes.

5. I have testified as an expert pharmacology or analytical chemistry witness nine (9) times over the past 22 years. *See* Attach. A at 106.

6. I obtained my B.A. in Chemistry, with honors, from Oberlin College in 1980. In 1985, I obtained my Ph.D. in Pharmacology from Johns Hopkins University School of Medicine, followed by a one-year postdoctoral fellowship, also at Johns Hopkins University School of Medicine.

7. After my postdoctoral fellowship, I served as an Assistant Professor of Chemistry, Member of the Biotechnology Faculty, and Director of a Mass Spectrometry Laboratory for Biotechnology Research at North Carolina State University from 1986 until 1993.

8. From 1994 until 2000, I was an Associate Professor in the Department of Medicinal Chemistry and Pharmacognosy at the University of Illinois College of Pharmacy. In 2000, I became Full Professor of Medicinal Chemistry and Pharmacognosy at the University of Illinois College of Pharmacy.

9. From 2011 until 2018, I also served as the Director of UIC/NIH Center for Botanical Dietary Supplements Research, University of Illinois at Chicago.

10. In 2018, I took on my current roles as a Professor of Pharmaceutical Sciences and Principal Investigator of the Linus Pauling Institute at Oregon State University.

11. I have authored or co-authored, and published, over 300 peer-reviewed articles, primarily in the areas of chemistry, medicinal chemistry, drug development, pharmacognosy, and pharmacology as described in my *curriculum vitae*. *See* Attach. A at 3-31.

12. I am currently conducting National Institutes of Health sponsored research into botanical dietary supplementation. My peer-reviewed research grants are described further in my *curriculum vitae*. *See* Attachment A at 107-118.

13. Throughout my career, I have served as the Editor-in-Chief or on the Editorial Board of several pharmacological and chemistry journals, including being on the Editorial Board of *Assay and Drug Development Technologies* since 2010 and the *Journal of the AOAC International* since 2016. I have also supervised over 80 graduate students and postdoctoral fellows in the areas of medicinal chemistry, chemistry, pharmacognosy, and pharmaceutical sciences during my career.

14. In my position, I routinely participate in the design and execution of clinical trials. I am the first author or co-author of over 10 peer-reviewed papers reporting results from clinical trials of dietary supplements. These studies include Phase I clinical trials as well as placebo controlled, randomized, double blind Phase II clinical trials.

15. As part of my academic pursuits, I routinely review and analyze clinical studies that evaluate the impact of a particular treatment on a particular condition. I also routinely review and analyze observational studies that observe correlations between certain indicators and certain

health outcomes. I have experience reviewing such studies to determine whether the study design limits the conclusions that may be drawn.

16. Based upon my education, training, and experience, as summarized above, I consider myself an expert in the fields of pharmacology, medicinal chemistry, and pharmacognosy with a comprehensive knowledge in the safety and efficacy of dietary supplements.

17. I am being compensated by the Department of Justice in this litigation at the rate of $300 per hour.

BACKGROUND

18. I understand that that Defendants Eric Nepute and Quickwork LLC sell Vitamin D and zinc supplements, including Wellness Warrior Vitamin D and Wellness Warrior Zinc. I also understand that Defendants sell other products containing Vitamin D and/or zinc, including Wellness Warrior Boost Pack, Wellness Warrior Immune Pack, and Wellness Warrior Kids' Multivitamin.

19. Wellness Warrior Vitamin D is a Vitamin D3[1] supplement. According to its Supplement Facts panel, Attachment U, one serving (one softgel capsule) of Wellness Warrior Vitamin D3 contains 125 mcg (5,000 IU) of vitamin D3 (Cholecalciferol). "Other ingredients" listed on the label are organic extra virgin olive oil and softgel (bovine gelatin, vegetable glycerin, and purified water).

20. Wellness Warrior Zinc is a zinc supplement. According to its Supplemental Facts panel, one serving (one tablet) of Wellness Warrior Zinc contains 25 mg of zinc (as Zinc

[1] Vitamin D3 is a form of Vitamin D. *See* Nat'l Inst. Of Health, Vitamin D: Fact Sheet for Consumers, *available at* https://ods.od.nih.gov/factsheets/VitaminD-Consumer/ (last visited Apr. 15, 2021).

Gluconate). "Other ingredients" listed on the label are Microcrystalline Cellulose, Dicalcium Phosphate, Stearic Acid, Colloidal Silicon Dioxide, Magnesium Stearate, and Croscarmellose Sodium.

21. I understand that, in this action, the Department of Justice alleges that Defendants Eric Anthony Nepute and Quickwork LLC advertised their products, Wellness Warrior Vitamin D and Wellness Warrior Zinc, by means of misrepresentations regarding the ability of Vitamin D and zinc, and by extension Wellness Warrior Vitamin D, Wellness Warrior Zinc, and other products containing Vitamin D or zinc, to treat and/or prevent COVID-19.

ASSIGNMENT

22. The Department of Justice asked me to evaluate, based on my expertise in the fields stated above, whether there is adequate scientific evidence to substantiate the following claims (collectively, "Wellness Warrior Advertising Claims"):

a. Vitamin D3, including Wellness Warrior Vitamin D3, treats, prevents, or reduces the risk of COVID-19;

b. Zinc, including Wellness Warrior Zinc, treats, prevents, or reduces the risk of COVID-19;

c. Vitamin D and zinc, including Wellness Warrior Vitamin D and Wellness Warrior Zinc, provide equal or better protection against COVID-19 than do currently available vaccines;

d. Vitamin D and zinc, including Wellness Warrior Vitamin D and Wellness Warrior Zinc, are scientifically proven to treat or prevent COVID-19;

e. People who have enough vitamin D, including Wellness Warrior D3, have a 52 percent lower risk of dying of COVID-19 than people who are deficient;

f. People who have enough Vitamin D, including Wellness Warrior D3, are 54 percent less likely to catch COVID-19;

g. That scientific publications indicate that people who have enough Vitamin D, including Wellness Warrior Vita D, are 77 percent less likely to catch COVID-19;

h. That Vitamin D, including Wellness Warrior Vita D, can block the COVID-19 spike protein from binding to the ACE2 receptor, thereby preventing infection; and

i. That Vitamin D, including Wellness Warrior Vita D, can prevent cytokine storm.

MATERIALS CONSIDERED

23. To assess the veracity of Defendants' claims, I reviewed certain sources that were provided to me by counsel. I understand that Defendants posted links to various documents to their website, www.wellnesswarrior.deals, under the heading "Vitamin D & Covid Research." I understand those sources were included in the materials that were provided to me. I also understand that counsel provided me with certain sources that were identified through review of Defendants' advertising videos, which occasionally contain references to specific studies.

24. I also performed a literature search to determine whether there is reliable scientific support for the Wellness Warrior advertising claims. I searched for published studies on COVID-19, its treatment, or the ingredients listed in Paragraphs 19-20, using PubMed, a database of more than 30 million citations for biomedical literature from MEDLINE, life science journals, and online books, maintained by the U.S. National Library of Medicine. Individuals employed in my field routinely use these sources to identify relevant research using the search method that I employed. In my experience, any relevant studies would be available through these

sources. I also searched for, and found no mentions of, "Wellness Warrior" or any of Defendants' products in the scientific literature.

25. A full list of materials that I considered is set forth in Attachment B.

ANALYSIS

A. Standards for Development of Reliable Scientific Evidence of Therapeutic Benefit

26. It is generally accepted by experts in the fields of pharmacology, medicinal chemistry, and pharmacognosy that, to adequately substantiate the efficacy of an intervention agent (such as the ingredients listed in Paragraphs 19-20) for treating, preventing, or reducing risks of COVID-19, there should, at a minimum, two or more clinical trials that meet or exceed the following standards—*i.e.*, competent and reliable scientific evidence:

a. First, the study must be a scientific peer-reviewed article. Prior to publication, editors of scientific journals require review of manuscripts by independent experts in the field being investigated. This approach provides quality control of the research literature.

b. Second, the study must be randomized, double-blinded, and placebo-controlled. In other words, study participants must be randomly assigned to one of two or more groups, the assignment of which is unknown to both the researchers and the participants, to assess the effect of the intervention without observational or clinical biases that might skew the results. The importance of controls in clinical trials is emphasized by the U.S. Food and Drug Administration in the document, *Drug Study Designs - Guidance for Institutional Review Boards and Clinical Investigators* (January 1998), which states as follows: "A well-controlled study permits a comparison of subjects treated with the new agent with a suitable

control population, so that the effect of the new agent can be determined and distinguished from other influences, such as spontaneous change, 'placebo' effects, concomitant therapy, or observer expectations." By randomly assigning participants to the placebo or intervention arm of a clinical trial, investigators can confidently isolate and measure the effect of the intervention. Blinding both the participants in the clinical trial as well as the investigators also helps control for bias in both the reporting and recording of results. If the participants and the investigators do not know whether the participants are receiving the treatment or the placebo, they cannot consciously or unconsciously change their evaluation of the relevant health outcome.

c. Third, the study must follow a prospective research design. Retrospective observational studies may be used to show an association between a product or ingredient and a health outcome, but they do not prove a causal link. Observational studies can help biomedical researchers develop hypotheses to test in prospective, randomized, double-blind, placebo-controlled clinical trials. A prospective clinical study is designed to address a particular research question by controlling variables that might interfere with the results and by including a sufficiently large number of participants to obtain a definitive answer. Retrospective studies obviously cannot change the parameters of the original prospective study design, and the investigators cannot be blinded.

d. Fourth, the study participants must be human. Research studies using *in vitro* or animal models can be suggestive of mechanisms or effects that may or may not be present in humans, but they do not, by themselves, provide adequate scientific

evidence for claims regarding the efficacy of such interventions when used by humans because of the differences in physiological systems.

e. Fifth, the study must use the product and dosage claimed to have the therapeutic effect.

f. Sixth, the endpoint of the study must be a measured effect on COVID-19 in humans.

g. Seventh, the study should be sufficiently powered to produce a statically valid result. The power of an experiment is the probability that the test will reject a false null hypothesis, in other words, confirm that two treatments produce different outcomes.

h. Eighth, the study should use a method of statistical analysis generally accepted by experts in the field.

27. Observational studies cannot be used to support a claim that a treatment confers some therapeutic benefit when used to treat a particular condition. This is because observations studies do not have the qualities of clinical trials as described above.

28. As set forth in more detail below, based on my review of the ingredients listed in Paragraphs 19-20 and my search of available scientific literature described in Paragraphs 23-24, I have identified no clinical trials that would satisfy the minimum requirements set forth in Paragraph 26 to support any of the Wellness Warrior Advertising Claims.

B. No Reliable Scientific Evidence Supports Claims That Vitamin D Can Treat Or Prevent COVID-19

29. Based on my review of the available literature, I have not identified any clinical trials showing that Vitamin D could protect against, treat, or prevent COVID-19 that would satisfy the minimum requirements set forth in Paragraph 26 above.

30. In the largest randomized clinical trial reported to date assessing Vitamin D as a treatment for COVID-19, Murai, *et al.*[2] found no beneficial effect to taking the supplement. In that study, 240 hospitalized COVID-19 patients were either administered a single oral dose of 200,000 IU Vitamin D or a placebo. The authors concluded, "Among hospitalized patients with COVID-19, a single high dose of [V]itamin D3, compared with placebo, did not significantly reduce hospital length of stay. The findings do not support the use of a high dose of [V]itamin D3 for treatment of moderate to severe COVID-19."

31. The remaining completed clinical trials that evaluated the potential of Vitamin D to treat or prevent COVID-19 are inconclusive pilot studies:

a. Ohaegbulam, *et al.*[3] published a case study in which 4 patients hospitalized with COVID-19 received either 1000 IU Vitamin D or 50,000 IU for 5 days. Although the 2 patients receiving the high dose of Vitamin D appeared to recover faster, the study was not randomized, not placebo-controlled, not blinded, and had too few participants to enable statistical evaluation of the outcome. There were also many uncontrolled variables. For example, only the 2 patients who received the lower dose of Vitamin D had a clinical history of diabetes and hypertension, which are comorbidities associated with more severe COVID-19. The authors acknowledged that, "Randomized clinical trials are recommended to validate the efficacy of [V]itamin D supplementation" due to the small size of the study.

[2] Murai, *et al.*, Effect of a single high dose of vitamin D3 on hospital length of stay in patients with moderate to severe COVID-19: A randomized clinical trial. *JAMA*. 2021, 325(11):1053-1060. doi: 10.1001/jama.2020.26848.

[3] Ohaegbulam *et al.*, Vitamin D supplementation in COVID-19 patients: A clinical case series. *Am. J. Ther*. 2020, 27(5):e485-e490. doi: 10.1097/MJT.0000000000001222.

b. Entrenas Castillo, *et al.*[4] administered oral Vitamin D to 50 out of 76 hospitalized COVID-19 patients, all of whom also received hydroxychloroquine and azithromycin. Some patients with pneumonia were also treated with the antibiotic ceftriaxone. While patients who received Vitamin D were admitted to the intensive care unit less frequently, the authors concluded that "[w]hether that would also apply to patients with an earlier stage of the disease and whether baseline Vitamin D status modifies these results is unknown." They also concluded that, "larger trials with [treatment and placebo] groups properly matched will be required to show a definitive answer." The study design had additional problems, including that: it was not blinded (it was an open-label study); it did not have placebo controls; and it did not give all patients the same drugs (although all were treated with hydroxychloroquine and azithromycin, only some patients received ceftriaxone). In addition, it did not measure the blood levels of Vitamin D, which would be necessary to support a causal relationship.

c. Rastogi, *et al.*[5] administered 60,000 IU Vitamin D or an unmatched placebo for 7 to 14 days to 16 participants with mild or asymptomatic SARS-CoV-2 infections. The mean number of days until each group tested negative for SARS-CoV-2 were identical at 17.6±6.1 and 17.6±6.4 days (p=0.283) in the intervention and control

[4] Entrenas Castillo, *et al.*, Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study. *J. Steroid Biochem. Mol. Biol*. 2020, 203:105751. doi: 10.1016/j.jsbmb.2020.105751.

[5] Rastogi, *et al.*, Short term, high-dose [V]itamin D supplementation for COVID-19 disease: a randomised, placebo-controlled, study (SHADE study). *Postgrad. Med. J.* 2020. doi:10.1136/postgradmedj-2020-139065

arm, respectively, which indicates that Vitamin D had no overall benefit. Nevertheless, the authors stated that more of the high-dose Vitamin D participants than unmatched placebo participants became SARS-CoV-2 RNA free by day 21. The authors noted the following limitations in their study, "We perceive certain limitations including that only mildly symptomatic and asymptomatic individuals were enrolled in the study which limits the generalisability of the results to symptomatic or severe cases of COVID-19. Placebo used in the study was not exactly matched with regards to the taste and consistency with the [Vitamin D] nano formulation. Also, the dose of [Vitamin D] used in the present study is high compared to conventional treatment." Another problem with the study design was that it was not double-blind (both investigators and patients knew who received Vitamin D or placebo).

d. Annweiler, *et al*.[6] reported a study of 66 nursing home residents, all of whom had been receiving single oral doses of 80,000 IU vitamin D3 every 2–3 months and all of whom were then diagnosed with COVID-19. Clearly, Vitamin D3 administration did not prevent COVID-19 in these patients. While the study participants who received Vitamin D either in the week following the diagnosis of COVID-19 or during the previous month had less severe symptoms, the authors noted that their study had many limitations. "First, the study cohort was restricted to a limited number of nursing-home residents who might be unrepresentative of all older adults. Second . . . no concerted efforts were made to systematically

[6] Annweiler, *et al.*, Vitamin D and survival in COVID-19 patients: A quasi-experimental study. *J. Steroid Biochem. Mol. Biol*. 2020, 204:105771. doi: 10.1016/j.jsbmb.2020.105771.

measure the serum 25(OH)D[7] concentration before and after supplementation. Third, the quasi-experimental design of our study is less robust than an RCT. Participants in the Comparator group did not receive vitamin D placebo, and there was no randomization." Because of these limitations, the investigators recognized the need to conduct an "RCT designed to test the effect of high-dose versus standard-dose vitamin D3 on 14-day mortality in COVID-19 older patients."

32. Because there are no qualified clinical trials that conform to the requirements of Paragraph 26 that demonstrate that Vitamin D can effectively treat or prevent COVID-19, there is no competent and reliable scientific evidence that Vitamin D can protect against, treat, or prevent COVID-19. Practitioners in my field would not conclude that it is scientifically proven that Vitamin D can protect against, treat, or prevent COVID-19.

33. Defendants' claim that individuals who have enough Vitamin D are 54 percent less likely to catch COVID-19 appears to be based on a study by Kaufman *et al*.[8] That study used a medical testing company's data to compare COVID-19 test results with circulating 25-hydroxyvitamin D levels (a measurement of Vitamin D concentration). It was a retrospective, observational study that, because of its study design, could not be used to determine whether low Vitamin D levels caused a greater risk of developing COVID-19, or whether taking Vitamin D supplements could reduce the risk of COVID-19 infection. Moreover, the study design compared COVID-19 test results to circulating 25(OH)D levels if the 25(OH)D levels were measured within *a year* of the COVID-19 test—a time lag that renders it impossible to assess whether the

[7] 25(OH)D, also known as hydroxyvitamin D, is a measurement of Vitamin D concentration in the blood.

[8] Kaufman, *et al.*, 2020. SARS-CoV-2 positively rates associated with circulating 25-hydroxyvitamin D levels. *PLosONE* 15(9): e0239252; https://doi.org/10.1371/journal.pone.0239252

patient had low [V]itamin D at the time he or she was diagnosed with COVID-19. The authors candidly acknowledged that the results of the "implications" for treatment from this study would be significant only "[i]f controlled trials find" the relationship between COVID-19 and Vitamin D "to be causative." In my opinion, this study does not support the claim that individuals who have enough Vitamin D are 54 percent less likely to catch COVID-19.

34. The basis of the claim that Vitamin D that reduces the risk of death from COVID-19 by 52% is unclear. I could find no reference citing this outcome. Defendants may be referring to the observational study by Maghbooli, *et al.*, which measured Vitamin D levels of 235 COVID-19 patients upon admission to a hospital in Iran.[9] In that study, 35 participants died, none of whom were under age 40. Out of these 33 deaths, 26 patients who died (16%) were identified as deficient in Vitamin D, whereas 7 deaths occurred in high Vitamin D patients (9%). According to this study, older patients with multiple health problems were at highest risk of death from COVID-19, and younger patients were protected regardless of Vitamin D status. Assuming that Vitamin D levels might be a factor—even though the data do not fully support this conclusion—the authors "recommended that further studies including RCTs are need be designed [*sic.*] to evaluate the role of [V]itamin D status on risk of developing COVID-19 infection and mitigating complications and mortality in those infected with the virus."

[9] Maghbooli Z *et al*., 2020. Vitamin D sufficiency, a serum 25-hydroxyvitamin D at least 30 ng/mL reduced risk for adverse clinical outcomes in patients with COVID-19 infection. *PLoS ONE* 15(9): e0239799. https://doi.org/10.1371/journal.pone.0239799.) The claim that Vitamin D reduces the risk of death from COVID-19 by 52% was made in a Daily Mail article that cited this study (the article referred to a 235-participant study performed in an Iranian hospital). *See* Daily Mail, *COVID-19 patients who get enough vitamin D are 52% less likely to die of the infection, study finds* (Sept. 25, 2020), https://www.dailymail.co.uk/health/article-8774015/Could-getting-vitamin-D-reduce-COVID-19-death-risks-52.html. I understand that Defendants repeated this claim in an email that was sent on September 26, 2020. *See* Complaint Ex. H.

35. The basis of the claim that people who have enough Vitamin D are 77 percent less likely to catch COVID-19 is also unclear. It may be based on an early draft of an observational study by Meltzer, *et al*.[10] This retrospective study compared Vitamin D levels measured up to a year previously to COVID-19 testing outcomes in patients at the University of Chicago. Although Vitamin D deficiency was associated with a positive COVID-19 test (1.77 relative risk[11]), ethnicity was the greatest risk of COVID-19 (2.54 relative risk), and most surprisingly, immunosuppressed patients (those who should be at greatest risk of infection) were found to be protected from COVID-19 (0.39 relative risk). The authors noted that "observed associations of vitamin D with outcomes in almost any observational study may fail to accurately reflect any potential causal effects of vitamin D on outcomes." The authors also concluded that "[r]andomized clinical trials of interventions to reduce Vitamin D deficiency are needed to determine if those interventions could reduce COVID-19 incidence." To put this study in perspective, a similar observational study found that Vitamin D levels upon hospital admission for COVID-19 had no correlation with clinical outcomes.[12] In my opinion, Meltzer, *et al*. does

[10] Meltzer *et al*., Association of vitamin D status and other clinical characteristics with COVID-19 test results. *JAMA Network Open*. 2020;3(9):e2019722. doi:10.1001/jamanetworkopen.2020.19722. The conclusions presented by the authors changed between an early draft of this study and the final, published version.

[11] As explained by the National Cancer Institute, relative risk is "a measure of the risk of a certain event happening in one group compared to the risk of the same event happening in another group." Nat'l Cancer Inst., Relative Risk, *available at* https://www.cancer.gov/publications/dictionaries/cancer-terms/def/relative-risk (last visited April 15, 2021).

[12] Jevalikar *et al*., Lack of association of baseline 25-hydroxyvitamin D levels with disease severity and mortality in Indian patients hospitalized for COVID-19. *Sci. Rep.* 11:6258. doi: 10.1038/s41598-021-85809-y.

not support the claim that people who have enough Vitamin D are 77 percent less likely to catch COVID-19.

36. Defendants claim that Vitamin D can prevent the SARS-CoV-2 spike protein from binding to the human cell receptor ACE2 and thereby prevent infection. During my review of the available literature, I did not identify any studies investigating live SARS-CoV-2, either in the human body or in a petri dish, which showed that Vitamin D can prevent infection of human cells through this mechanism. The only study that I was able to identify that addressed Vitamin D's ability to prevent the SARS-CoV-2 spike protein from binding to the ACE2 receptor was a theoretical study that used computer models of the chemical structures of the SARS-CoV-2 spike protein and various small molecules to predict that Vitamin D (as well as steroids and retinoids) might bind to the spike protein.[13] However, this study did not determine whether: (i) Vitamin D binds to the spike protein in the real world; (ii) Vitamin D prevents binding of SARS-CoV-2 to ACE2 of human cells; (iii) Vitamin D prevents SARS-CoV-2 from infecting human cells; or (iv) Vitamin D prevents COVID-19 through this mechanism. There is no competent and reliable scientific evidence that Vitamin D can prevent the SARS-CoV-2 protein from binding to the ACE2 receptor of human cells.

37. Defendants claim that Vitamin D can prevent the cytokine storm, which is a severe immune response in COVID-19 patients that can cause respiratory failure and death. I found no evidence that treatment of COVID-19 patients with Vitamin D has been shown to prevent such severe cytokine responses. A review article addressing available research regarding

[13] Shoemark *et al.*, Molecular simulations suggest vitamins, retinoids and steroids as ligands of the free fatty acid pocket of the SARS-CoV-2 spike protein. *Angew. Chem. Int. Ed. Engl*. 2021, 60, 7098-7110. doi: 10.1002/anie.202015639..

this topic concluded only that "[f]urther research is needed to understand the effects of Vitamin D and the various cytokines prevalent among endotypes of nasal/pharyngeal illnesses on COVID-19 pathogenesis."[14] Another review article on this topic concluded:

> We speculate that [V]itamin D *might* alleviate lung injury induced by SARS-CoV-2 by upregulating ACE2, decreasing inflammatory cytokines, and increasing antimicrobial peptides. *The efficacy of [V]itamin D in treatment of SARS-CoV-2 needs to be verified through more evidence-based medicine*. In the future, we hope that randomized controlled clinical trials can be carried out to achieve this.[15]

There is no competent and reliable scientific evidence showing that Vitamin D can prevent cytokine storm.

38. In sum, there are no well-designed clinical studies that support any of Defendants' claims regarding Vitamin D, and by extension Wellness Warrior Vitamin D. Accordingly, there is no competent and reliable scientific evidence substantiating any of the Wellness Warrior Advertising claims relating to Vitamin D.

C. **No Reliable Scientific Evidence Supports Claims That Zinc Can Treat or Prevent COVID-19**

39. Based on my review of the available literature, I have not identified any clinical trials showing that zinc could protect against, treat, or prevent COVID-19 that would satisfy the minimum requirements set forth in Paragraph 26 above. On the contrary, Thomas, *et al.*,[16] the only such clinical trial that I identified, reported a clinical trial of outpatients with COVID-19

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[14] Jain *et al.*, Biomolecular endotype factors involved in COVID-19 airway infectivity: A systematic review. *Auris Nasus Larynx*. 2021 Feb;48(1):32-40. doi: 10.1016/j.anl.2020.11.006.

[15] Xiao *et al.*, Could SARS-CoV-2-induced lung injury be attenuated by vitamin D? *Int. J. Infect. Dis*. 102 (2021) 196-202. doi: 10.1016/j.ijid.2020.10.059.

[16] Thomas, *et al.*, Effect of high-dose zinc and ascorbic acid supplementation vs usual care on symptom length and reduction among ambulatory patients with SARS-CoV-2 infection: the COVID A to Z randomized clinical trial. *JAMA Netw. Open.* 2021:4(2).e210369. doi:10.1001/jamanetworkopen.2021.0369

that found no benefit for zinc treatment. In this study, 214 outpatients diagnosed with COVID-19 were randomized to one of four groups as follows: high-dose zinc; ascorbic acid (Vitamin C); high-dose zinc plus ascorbic acid; or no intervention except the standard of care. No difference in recovery time was observed between treatment groups.

40. Therefore, there is no competent and reliable scientific evidence to support the claim that zinc can prevent against, treat, or prevent COVID-19. Practitioners in my field would not consider it scientifically proven that zinc can protect against, treat, or prevent COVID-19.

D. No Reliable Scientific Evidence Supports Claims That Vitamin D or Zinc Provide Equal Or Better Protection Against COVID-19 Than Do Currently Available Vaccines

41. Since the beginning of the COVID-19 pandemic, 12 vaccines have progressed from Phase I clinical trials of safety through Phase III clinical trials of efficacy.[17] Enrolling from 10,000 to over 40,000 participants each, these vaccines have shown efficacy ranging from 50.4% to 95% in preventing COVID-19 and efficacy as high as 100% in preventing severe COVID-19.

42. These vaccine studies were well-designed, placebo-controlled, blinded clinical trials that complied with the requirements set forth in Paragraph 26 above. For example, BioNTech and Pfizer are collaborating on the development and clinical evaluation of a messenger-RNA based vaccine. Their clinical design is posted on clinicaltrials.gov as study number NCT04368728. Still on-going, this large study includes 43,998 healthy participants in Phase 1, Phase 2, and Phase 3 clinical trials that are randomized, placebo-controlled, and triple-blinded (participant, care provider, and investigator). The Phase 1 study was designed to identify a preferred candidate and dose level for one of 3 SARS-CoV-2 RNA vaccines. The Phase 2/3

[17] Funk, *et al.*, Target product profile analysis of COVID-19 vaccines in phase III clinical trials and beyond: An early 2021 perspective. *Viruses*. 2021 Mar 5; 13:418. doi: 10.3390/v13030418.).

study is using larger numbers of participants to evaluate efficacy, safety, and tolerability of a SARS-CoV-2 RNA vaccine against COVID-19. So far, at least 3 peer-reviewed scientific publications have resulted from these clinical trials.[18]

43. As discussed above, there are no similar studies demonstrating any therapeutic benefit from taking Vitamin D or zinc for the prevention or treatment of COVID-19. Accordingly, there is no competent or reliable scientific evidence that Vitamin D or zinc provide equal or better protection against COVID-19 than do currently available vaccines. Practitioners in my field would not consider it proven that Vitamin D or zinc provide equal or better protection against COVID-19 than do currently available vaccines.

CONCLUSION

44. Based on my review and analysis of available scientific evidence, it is my expert opinion that there is no competent and reliable scientific evidence to support the Wellness Warrior Advertising Claims. Practitioners in my field would not consider the Wellness Warrior Advertising Claims to be adequately substantiated.

I declare under penalty of perjury that the foregoing statement is true and correct.

Executed on April 15, 2021. Richard B. van Breemen

Richard B. van Breemen

[18] Polack, *et al.*, C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N. Engl. J. Med.* 2020 Dec 31;383(27):2603-2615. doi: 10.1056/NEJMoa2034577. Walsh, *et al.*, Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. *N. Engl. J. Med.* 2020 Dec 17;383(25):2439-2450. doi: 10.1056/NEJMoa2027906. Mulligan, *et al.*, Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature*. 2020 Oct; 586(7830):589-593. doi: 10.1038/s41586-020-2639-4.